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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/621,593	07/21/00	DE GROOT	N 4497US

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EXAMINER	
WHITEMAN, B	
ART UNIT	**PAPER NUMBER**
1633	11

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/621,593	DE GROOT ET AL.	
	Examiner	Art Unit	
	Brian Whiteman	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 September 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-14,17-19 and 22-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-14,17-19 and 22-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Non-Final Rejection

Priority

No priority is claimed.

Sequence compliance

On pages 14 and 15 of the specification, the specification contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 because the specification does not label the sequences and the applicants' have not provided a paper and a disk copy of the sequences. Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825). Thus, applicants' are required to submit a paper and a disk copy of the sequences in compliance with PTO guidelines prior to or with response to this office action.

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Claims 15 and 16 were cancelled in paper no. 6 filed on 5/11/01.

Cancellation of claims 2, 20, and 21 is acknowledged and the addition of claims 23-25 is acknowledged in paper no. 10 filed on 9/27/01 and no new matter was added.

Applicants' election of Group I in Paper No. 10 is acknowledged. Applicants' election without traverse of Group I in Paper No. 10 is acknowledged. Furthermore, applicants amended

claims of Groups II (claims 1, 3-9, and 22) to read on the elected embodiment as requested by examiner in paper no. 7 filed on 7/25/01 is acknowledged.

Claim Objections

Claims 7 and 22 are objected to because of the following informalities: grammatical error in the phrase "promoter capable of driving expression of said protein essentially specifically in said cell". Suggest amended the phrase to state 'tissue-specific promoter capable of driving expression of said protein in said cell". Appropriate correction is required.

Claims 1, 3-14, 17-19 and 22-25 are pending examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-14, 17-19 and 22-25, as best understood, are readable on a starting material consisting of a protein that is capable of transporting a member of a first class of immunoglobulin from the cell's basolateral side to the cell's apical side, wherein a genus of the protein and the genus of a transgenic non-human farm animals comprising the protein, and wherein the genus of the non-human farm animal or the genus protein are not claimed in a specific biochemical or molecular structure that could be envisioned by one skilled in the art at the time the invention was made is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Claims 18 and 19, as best understood, are readable on a genus of a substance capable enhancing expression of a nucleic acid encoding said protein, wherein said genus of a substance is not claimed in a specific biochemical or molecular structure that could be envisioned by one skilled in the art at the time the invention was made is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The specification contemplates production of non-human animals, wherein the non-human animal's cells comprise a recombinant nucleic acid encoding a protein capable of transporting any immunoglobulin from the cell's basolateral side to the cell's apical side. The specification provides sufficient guidance of a species of a protein capable of transporting an immunoglobulin gene from the basolateral side of a cell to the apical side of the same cell. On page 13 of the application, the specification uses a protein polymeric immunoglobulin receptor (pIgR)) capable of transporting a murine dimeric IgA (dIgA) from the basolateral side to the apical side of murine mammary epithelial cells. Furthermore, the as-filed specification cites an IgG1 receptor, which carries gammaglobulins (IgGs) from a mother to her young via a neonatal intestine (page 6).

The specification contemplates a substance capable of enhancing expression of a nucleic acid encoding said protein. The disclosure provides sufficient description of a species consisting of proteins selected from interferon γ, interleukin-1, interleukin-4, and tumor necrosis factor-α.

However, it is apparent that on the basis of the applicants' disclosure that an adequate written description of the invention defined by the claims requires more than a mere statement

that it is part of the invention and reference to potential methods and/or molecular structures of molecules that are essential for the genus of proteins that are capable of transporting an immunoglobulin from the basolateral side of a cell to the apical side of the cell; or a substance capable of enhancing expression of a nucleic acid encoding said protein; what is required is the knowledge in the prior art and/or a description as to the availability of a representative number of the species of biochemical or molecular structures of proteins or substances that must exhibit the disclosed biological function as contemplated by the claimed invention.

It is not sufficient to support the present claimed invention directed to a genus of a transgenic non-human animal comprising a protein that is capable of transporting any immunoglobulin from the cell's basolateral side to the cell's apical side, a genus of protein that is capable of transporting any immunoglobulin from the cell's basolateral side to the cell's apical side or a genus of a substance capable of enhancing expression of a nucleic acid. The claimed invention as a whole is not adequately described if the claims require essential or critical elements, which are not adequately described in the specification and which is not conventional in the art as of applicant's effective filing date. Claiming unspecified proteins or unspecified substances that must possess the biological properties as contemplated by applicant's disclosure without defining what means will do so is not in compliance with the written description requirement. Rather, it is an attempt to preempt the future before it has arrived. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)). Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics such that a person skilled in the art would recognize that the

inventor had possession of the claimed invention. Pfaff v. Wells Electronics, Inc., 48 USPQ2d 1641, 1646 (1998). The skilled artisan cannot envision the detailed structure of a genus of the claimed non-human animal wherein a cell of said animal comprises a recombinant nucleic acid encoding a protein capable of transporting an immunoglobulin form the cell's basolateral side to the cell's apical side, and/or proteins that must exhibit the contemplated biological functions, or substances that must exhibit the contemplated biological functions, and therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the structures and/or methods disclosed in the as-filed specification. Thus, in view of the reasons set forth above, one skilled in the art at the time the invention was made would not have recognized that applicant was in possession of the claimed invention as presently claimed.

Claims 1, 3-14, 17-19 and 22-25 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Specifically, since the claimed invention is not supported by a sufficient written description (for possession of a genus of a protein capable of transporting a member of an immunoglobulin from the cell's basolateral side to the cell's apical side or a genus of substances capable of enhancing expression of a nucleic acid encoding said protein), particularly in view of the reasons set forth above, one skilled in the art would not have known how to use and make the claimed invention so that it would operate as intended, e.g. function in a cell comprising the protein in an amount that is at least 10-fold higher than an endogenously expressed analogous and/or homologous immunoglobulin transporter protein.

In addition, the specification discusses that the claimed embodiment features a transgenic non-human farm animal wherein a cell of said animal comprises a recombinant nucleic acid encoding a protein capable of transporting an immunoglobulin from the cell's basolateral side to the cell's apical side (pages 2 and 3). The specification provides teachings pertaining to the pIgR that is capable of transporting dimeric IgA across the epithelial cells of mucosal surfaces into the external secretions and thereby capable of raising the concentration of IgA relative to IgG in external secretion (pages 6 and 7).

However, the specification fails to provide any relevant teaching or specific guidance with regard to the generation of a transgenic animal comprising a recombinant nucleic acid encoding a protein capable of transporting an immunoglobulin from the cell's basolateral side to the cell's apical side other than transgenic mice. Furthermore, the specification fails to provide sufficient guidance in particular to a non-human animal, which expresses the protein such that a phenotype occurs (phenotype that would display a non-free disease phenotype). Also, the specification fails to even describe any particular type of phenotype exhibited by a transgenic non-human animal of the claimed invention, such that the animal would be useful as a model for better protection against an invasion and/or colonization of mucosal surfaces by a pathogen (page 3). Thus, as enabled requires the specification to teach how to make and use the claimed invention, the specification fails to enable the production of any transgenic non-human animal comprising a protein that is capable of transporting an immunoglobulin from the cell's basolateral side to the cell's apical side for use as a model for protection against an invasion and/or colonization of mucosal surfaces by a pathogen.

[Note that although the claimed transgenic non-human farm animal is not limited to expression of the protein at a level resulting in a specific phenotype, with regard to the claims breadth, the standard under 35 U.S.C. 112, first paragraph, entails the determination of what claims recite and what the claims mean as a whole. In addition, when analyzing the enabled scope of the claims, the teachings of the specification are to be taken into account because the claims are to be given their broadest reasonable interpretation that is consistent with the specification. As such, the broadest interpretation of the claimed transgenic non-human farm animal having cells, which harbor a recombinant nucleic acid that expresses the protein at a level sufficient to result in a specific phenotype (i.e., it is unknown what other purpose the transgenic animal would serve if the transgene is not expressed at a sufficient level for a resulting phenotype).]

As the specification fails to provide any relevant teachings or guidance with regard to the production of a transgenic non-human farm animal as claimed other than mice, the mouse model can only be used for future experimentation and research, one skilled in the art would not be able to rely on the state of the art for an attempt to produce a representative number of transgenic non-human farm animals possessing the protein of interest and being enabled for a non-free disease phenotype. This is because the state of the art of transgenics is not predictable with respect to transgene behavior and the resulting phenotype. While the state of the art would be able to produce transgenic non-human farm animals comprising the recombinant nucleic acid of interest; it is not predictable if the transgene would be expressed at a level and specificity to cause a particular phenotype (non-free disease phenotype). For example, the level and the specificity of expression of a recombinant nucleic acid as well as the resulting phenotype of the transgenic

non-human animal are directly dependent on the specific transgene construct. A recombinant nucleic acid of interest, a promoter, an enhancer, coding or non-coding sequences present in the transgene construct, the specificity of the transgene integration into the genome, are all important factors in controlling the expression of a recombinant nucleic acid in the production of a transgenic non-human animal, which exhibits a resulting phenotype. This observation is supported by Wall (theriogenology, 1996) who states, "Our lack of understanding of essential genetic control elements makes it difficult to design transgene with predictable behavior (page 61, last paragraph)." Also, Houdebin discloses that in the field of transgenics, constructs must be designed case by case without general rules to obtain good expression of a transgene (Journal of Biotechnology, page 275, column 1, 1994); e.g. specific promoters, presence or absence of introns, etc. As such guidance is lacking in the as-filed specification, it fails to feature any reasonable correlation between the over-expression of the recombinant nucleic acid encoding the pIgR protein to any other non-human animal, and furthermore does not provide a specific resulting phenotype for the transgenic mice.

Furthermore, without evidence to the contrary, transgene expression in different species of transgenic animals (e.g. farm animals) is not predictable and varies according to the particular host species and the specific promoter/gene combination. This observation is specifically supported by Hammer et al. (Journal of Animal Science, 1986), Hammer reports that the production of transgenic mice, sheep, and pigs; only transgenic mice exhibited an increase in growth due to the expression of the gene encoding human growth hormone (pages 276-277, subsection: Effect of Foreign GH or Growth). The same transgene construct in transgenic pigs and sheep did not cause the same phenotypic effect. Also see Ebert et al (Molecular

Endocrinology, 1988). This observation is supported by Mullins et al. (Journal of Clinical Investigations, 1996), Mullins states "a given construct may react very differently from one species to another (page S39, Summary)." Wall et al. report "transgene expression and the physiological consequences of transgene products in livestock are not always predicted in transgenic mouse studies (page 62)." Kappel et al disclose the existence of inherent cellular mechanisms that may alter the pattern of expression such as DNA imprinting, resulting in differential CpG methylation (Current Opinion in Biotechnology, page 549, column 2). Strojek and Wagner (Genetic Engineering, 1988, pages 238-239). Given such species differences in the expression of a transgene, particularly when taken with the lack of sufficient guidance in the disclosure for the production of a representative number of transgenic non-human animals whose genome comprises a protein capable of transporting an immunoglobulin from the cell's basolateral side to the cell's apical side, it would require an undue amount of experimentation to reasonably predict the results achieved in any other non-human animal besides mice comprising the expression of a protein (e.g. pIgR), the levels of the transgene product, the consequences of the production, and therefore, the resulting phenotype (non-free disease phenotype).

In addition, with respect to the breadth of claim 3 comprising a recombinant nucleic acid in the cells of the transgenic non-human farm animal, it is noted that the claimed embodiment encompasses a protein (e.g. pIgR) comprises a polymeric immunoglobulin receptor or a functional part, derivative, and/or analogue thereof. Since, the relationship between a sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable (e.g. see Chiu et al., *Folding and Design*, 1998, pp. 23-228), it would required undue experimentation for one skilled in the art to arrive at other proteins comprising the same

biological function as a polymeric immunoglobulin receptor (e.g. pIgR). In addition, the as-filed specification does not provide sufficient guidance or reasonable correlation for teaching the production of any other transgenic non-human animal whose genome comprises and over-expresses a polymeric immunoglobulin receptor other than a fully functional murine pIgR in a transgenic mouse and the specification does not display a corresponding phenotype. However, if the disclosure provides a showing or reasonable correlation teaching evidencing the production of a representative number of non-human transgenic animals whose genomes comprise and over-express a pIgR transgene, and thus, exhibiting a corresponding phenotype, then the enabled scope of the claimed invention would be limited to that particular transgene, and not the numerous functional part, derivative, and/or analogue thereof. In view if of references cited above, the state of the art supports that transgene behavior is unpredictable and thus, would be critical to the resulting phenotype. Thus, the claimed invention is only enable for a transgenic mouse, wherein an epithelial cell of said mouse comprises a recombinant nucleic acid encoding murine pIgR protein, wherein the protein is capable of transporting IgA from the cell's basolateral side to the cell's apical side.

Furthermore, with respect to the breadth of the claimed embodiment encompassing a protein capable of transporting an immunoglobulin from the cell's basolateral side to the cell's apical side, the specification and the state of the art lack sufficient guidance for using any cell (*e.g.* liver, brain, muscle, etc.) in a transgenic non-human farm animal other than epithelial cells. The state of the art displays that the polyimmunoglobulin receptor is expressed in several tissues such as the intestine, kidney, lung, and liver (DeGroot et al. Transgenic Research, Vol. 8, page 126, 1999). However, the specification does not reasonably correlate from generating transgenic

mice over-expressing the murine pIgR in their mammary glands (epithelial cells) to any other tissue. For example, human hepatocytes do not express pIgR (Lamm, Am. J. Physiol, Vol. 37, G614-G617, 1998). In view of the concerns discussed above regarding the unpredictability of producing transgenic animals it would require an undue amount of experimentation to make and/or use any other cell that expresses a protein that is capable of transporting an immunoglobulin from the cell's basolateral side to the cell's apical side other than epithelial cells. Thus, the claimed invention is not enabled for any cell other than epithelial cells.

In addition, with respect to claims that encompass providing a cell of a transgenic non-human with a nucleic acid encoding a protein capable of transporting a member of said first class of immunoglobulin from the cell's basolateral side to the cell's apical side, the claims are not enabled for any immunoglobulin other than IgA and IgM because only IgM and IgA are able to pass through the epithelial layer and enter the secretion in a significant amount (Lamm, G614). Lamm teaches:

> immunoglobulins that are not polymeric, such as IgG, the major class of antibody in serum, have no physiological means of reaching the external secretions. They do not bind to the pIgR, and, like macromolecules generally, they are prevented from diffusing through the epithelium by the tight junctions that connect adjacent epithelial cells (G614).

Also, with respect to claims 17-19 that encompass a method for collecting an immunoglobulin from a non-human animal. The claims read on an in vivo and an in vitro method for collecting an immunoglobulin from a non-human animal and as stated above the claims are not enabled for any transgenic non-human due to lack of sufficient guidance for providing a phenotype (non-free disease). In addition with respect to an in vivo method, the

specification and the state of the art lack sufficient guidance for targeting a specific cell in a non-human animal because it would take one skilled in the art an undue amount of experimentation to determine how to make and/or use a nucleic acid encoding a protein of interest that could be administer to the non-human animal and specifically target a secretory cell (See Anderson), The state of the art exemplified by Anderson et al., *Nature*, Vol. 392, pp. 25-30, April 1998, displays major consideration for any gene transfer or any DNA therapy protocol involve issues that include:

1) The type of vector and amount of DNA constructs to be administered,

2) The route and time course of administration, the sites of administration, and successful uptake of the claimed DNA at the target site;

3) The trafficking of the genetic material within cellular organelles, the rate of degradation of the DNA, the level of mRNA produced, the stability of the mRNA product, the amount and stability of the protein produced, and

4) What amount of the expressed proteins considered to be therapeutically effective for a DNA therapy method (Anderson, *Nature*, Vol. 392, pp. 25-30, April 1998).

In addition, all of these issues differ dramatically based on the specific vector used, the route of administration, the animal being treated, therapeutically effective amount of the DNA, and the disease being treated.

Anderson teaches that gene therapy is a powerful new technology that still requires several years before it will make a noticeable impact on the treatment of disease, and that several major deficiencies still exist including poor delivery systems, both viral and non-viral, and poor gene expression after genes are delivered (pp. 25-30). Anderson further teaches that the reason

for the low efficiency of gene transfer and expression in human patients is that we still lack the basis understanding of how vectors should be constructed what regulatory sequences are appropriated for which cell types (page 30, column 1, last paragraph). Furthermore with respect to the in vivo method, the disclosure fails to provide how one skilled in the art could collect the secretory fluid produced by the cell and/or the tissue said cell is part of and obtaining said immunoglobulin. Thus, claims 17-19 are not enabled by the disclosure.

In addition with respect to claims 9 and 25 that encompass the method of 1, wherein said cell comprises said protein in an amount that is at least 10-fold higher than an endogenously expressed analogous and/or homologous immunoglobulin transporter protein. The claims are not enabled because in view of the concerns listed above encompassing the lack of sufficient guidance for making and/using any protein other than pIgR, the disclosure, and the state of the art, the disclosure lacks sufficient guidance for defining what proteins are endogenously expressed analogous and/or homologous immunoglobulin transporter protein other than pIgR and IgG1 receptor. Furthermore, the specification does not provide sufficient guidance for how to make and/or use a protein in an amount that is at least 10-fold higher than any endogenously expressed analogous and/or homologous immunoglobulin transporter protein other than pIgR in mice. Therefore, the claims are not enabled for using any protein in an amount that is at least 10-fold higher than any endogenously expressed analogous and/or homologous immunoglobulin transporter protein other than pIgR in mice because it would take one skilled in the art an undue amount of experimentation to determine what other proteins are endogenously expressed analogous and/or homologous immunoglobulin transporter protein.

In conclusion, the as-filed specification and claims coupled with the state of the art at the time the invention was made do not enable one skilled in the art to make and/or use any part of the claimed invention. Given that the production of producing transgenic animals and their respective phenotypes were unpredictable at the time the invention was made, and given the lack of sufficient guidance or direction provided the specification for the production of any transgenic animal other then the transgenic mice expressing a murine pIgR, one skilled in the art would have to engage in a large quantity of experimentation in order to practice the claimed invention based on the applicant's disclosure and the unpredictability of making transgenic animals.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 7, 17-19, 22, and 24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The phrase "a functional equivalent of said cell" in claims 7, 22, and 24 is a relative term, which renders the claim indefinite. The phrase "a functional equivalent of said cell " is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is unclear what is a functional equivalent of said cell and the disclosure does not define the metes and bounds of the phrase. Clarification is requested.

Claims 7, 22, and 24 are objected to under MPEP 2173.05(h), as using improper Markush group language. The claims recite, "in said cell and/or a functional equivalent of said cell." The

term "and/or" is an unacceptable Markush group language. Suggest amending the claim to "in said cell or a functional equivalent of said cell."

Claims 17-19 are vague and indefinite for failing to define whether the administration is a step before or after providing a secretory cell of said animal, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The metes and bounds of how the claims are linked are not defined by the disclosure. Clarification is requested.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The claimed invention is not enabled due to the failure of the specification to describe any particular type of phenotype exhibited by a transgenic non-human farm animal of the claimed invention, such that the animal would be useful as a model for better protection against an invasion and/or colonization of mucosal surfaces by a pathogen. However, one skilled in the art would understand that the claimed embodiment also reads on a method for studying the over-expression of murine pIgR in transgenic mice for immunology, cell physiology and cell biology research purposes. Thus, the following prior art rejection is directed to transgenic mice, for use in research, wherein a cell of said mice comprises a recombinant nucleic acid encoding the pIgR protein capable of transporting the immunoglobulin (IgA) from the epithelial cell's basolateral side to the cell's apical side.

Claims 1, 3, 4, 8, 11, 13, 14, and 22-25 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by DeGroot et al. (Transgenic Research, Vol. 8, pages 125-135, April 1999). DeGroot generated four different transgenic mice lines over-expressing the murine pIgR gene at 10-30 fold increased mRNA levels, relative to the endogenous mRNA levels in their mammary glands (page 126). The transgene (pIgR) was expressed in the mammary gland in a tissue specific manner an only during lactation (page 126). The secretory component (SC) protein levels in the milk of the four transgenic lines were increased 10-270 fold compared to endogenous SC protein levels (page 126).

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ms. Tracey Johnson whose telephone number is (703) 305-2982. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (703) 305-0775. The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Clark can be reached at (703) 305-4051.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 308-2742.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Brian Whiteman
Patent Examiner, Group 1633
October 21, 2001

DAVE T. NGUYEN
PRIMARY EXAMINER